macrophage-derived cell lines *in vitro* as well as death when injected intravenously.

Indirect evidence had suggested that LF was a metalloprotease. However, the intracellular target of LF remained unknown until recently when NIH scientists discovered that LF proteolytically inactivates mitogen activated protein kinase kinase 1 and 2 (MAPKK1, 2). Using oocytes of the frog *Xenopus laevis* as well as tumor derived NIH3T3 (490) cell expressing an effector domain mutant form of the human V12HaRas oncogene these scientists demonstrated that LF induced proteolysis of MAPKK 1 and 2, resulting in their irreversible inactivation. MAPKK 1 and 2 are components of the mitogen activated protein kinase (MAPK) signal transduction pathway, an evolutionarily conserved pathway that controls cell proliferation and differentiation in response to extracellular signal and also plays a crucial role in regulating oocyte meiotic maturation. Further, the MAPK pathway has been shown to be constitutively activated in many primary human as well as in tumor-derived cell lines. Consistent with this, treatment of V12Ha–Ras transformed NIH 3T3 cells with LeTx inhibits cell proliferation and causes their reversion to a non-transformed phenotype.

This invention specifically relates to *in vitro* and ex vivo methods of screening for modulators, homologues, and mimetics of LF mitogen activated protein kinase kinase (MAPKK) protease activity. Applications for this technology could be:

1. A novel tool (LF) for the study of the cellular role of the MAPK pathway in normal or tumor cells.

2. Investigation of LF for developing inhibitors for cancer therapy. By analyzing structural-functional relationships, additional compounds with improved specificity, increased potency, and reduced toxicity can be generated. Mimetics which block MAPKK activity or the determination of mechanisms of regulation of proteases that target MAPKK at or near the same site targeted by LF could be developed.

3. A protease-based assay for LF by using a peptide to test for LF cleavage. There is no commercial test for anthrax. This assay could be used for testing soldiers for anthrax exposure. Characterization of the interaction between LT and MAPKK at the amino acid level may lead to the generation of inhibitors which may prove useful in treating anthrax.

The above mentioned invention is available for licensing on an exclusive or non-exclusive basis.

Dated: March 5, 1999.

Jack Spiegel,

Director, Division of Technology Development and Transfer, Office of Technology Transfer.

[FR Doc. 99–6205 Filed 3–12–99; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, Public Health Service, DHHS.

ACTION: Notice.

SUMMARY: The inventions listed below are owned by agencies of the U.S. Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 207 to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

ADDRESSES: Licensing information and copies of the U.S. patent applications listed below may be obtained by writing to Girish C. Barua, Ph.D. at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852–3804; telephone: 301/496–7057 ext. 263; fax: 301/402–0220; e-mail: gb18tnih.gov. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

Mixing Arrangement and Method

Lesley Pesnicak (NIAID)
Serial No. 08/823,417 filed 25 Mar 97; U.S. Patent 5,810,773 issued 22 Sep 98

An arrangement for sterilely mixing two viscous fluids together. It consists of a base with removable stops to accommodate two syringes (different sizes can be used) and a 3-way stopcock. Two commercially available syringes are connected to a 3-way stopcock and fitted onto the base such that the flanges of the syringes are up against stops connected to the base and the 3 way stopcock is fitted into stops also connected to the base in such a manner that syringes and stopcock are unable to pull apart when the desired fluids are forced through the stopcock from one syringe to another. In this manner two fluids can be easily mixed without the loss for material which might result from the syringes popping off the stopcock and the ability to provide complete sterility. This device is especially good for emulsification of peptides.

Isolation of Amplified Genes Via cDNA Subtractive Hybridization

Bertrand C. Liang (NCI)
Serial No. 08/700, 763 filed 09 Aug 96; U.S. Patent 5,827,658 issued 27 Oct 98

A method of analyzing an amplified gene, including determining its copy number involves subtractive hybridization of cDNA libraries, one from the tissue of interest and the other containing biotinylated cDNA from normal tissue, where the annealed cDNA is removed by means of magnetic beads coated with streptevidin or avidin. The cDNA isolated after subtractive hybridization represents amplified DNA, and it is analyzed to determine what gene(s) were amplified. Furthermore, the copy number of the gene(s) can be estimated. The copy number thus determined can be correlated to the severity of a pathogenic state, to the prognosis or to treatment efficacy.

Method of Identifying and Using Drugs With Selective Effect Against Cancer Cells

George F. Vande Woude, Anne P. Monks, Han-Mo Koo (NCI) Serial No. 08/260,515 filed 15 Jun 94; U.S. Patent 5,645,983 issued 08 Jul 97

The invention covers a method of identifying drugs which selectively inhibit the growth of particular cancer cells. This is accomplished by contacting cancer cells, which differ as to the presence of a particular DNA sequence with a drug and measuring the effect of the drug on growth of the cells. A determination is then made as to whether there is a correlation between the growth rate and presence or absence of the DNA sequence.

The invention may potentially be applied in research and development of cancer therapeutics, or as a diagnostic. It may provide the ability to design combinations of drugs for cancer treatment.

Dated: March 5, 1999.

Jack Spiegel,

Director, Division of Technology Development and Transfer, Office of Technology Transfer.

[FR Doc. 99–6206 Filed 3–12–99; 8:45 am]

BILLING CODE 4140–01–M